ISSN: 1607-8322, e-ISSN: 2220-5799 **Anaesthesia, Pain & Intensive Care**
Vol 25(5); October 2021 DOI: 10.35975/apic.v25i5.1636

CASE REPORT **ANESTHESIA & CONCURRENT DISEASE**

Anesthetic management of a patient with known Dubin Johnson Syndrome – a case report

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Abstract

This is a case report of the anesthetic management of a 20-year-old woman, a known case of Dubin Johnson syndrome (DJS). The patient underwent laparoscopic appendicectomy under general anesthesia. Aside from elevated serum bilirubin levels, other routine laboratory tests were normal.

As it is a rare and uncommon disease, the anesthetic management was considered a challenge. Liver being the organ affected, the drugs, which increases bilirubin, were to be avoided. Selection of drugs to provide analgesia, anesthesia and to reduce perioperative stress was a priority and to prevent the rise in bilirubin levels.

Key words: Dubin Johnson syndrome; Anesthesia management; Liver enzymes

Citation: John AA, Shibli KU, Soliman MH, Elboursaly I, Ramanathan L. Anesthetic management of a patient with known Dubin Johnson Syndrome – a case report. Anaesth. pain intensive care 2021;25(5):676–679;

DOI: 10.35975/apic.v25i5.1636

Received: April 25, 2021; **Reviewed:** May 6, 2021; **Accepted:** June 11, 2021

1. Introduction

Dubin Johnson syndrome (DJS) is a rare autosomal recessive benign disease characterized by familial idiopathic jaundice with chronic intermittent conjugated hyperbilirubinemia and normal transaminases.

The main findings of the disease are hepatomegaly associated with abdominal pain and jaundice.[1] The usual onset of DJS is in early adulthood presenting with non-pruritic jaundice that is caused by increased conjugated hyperbilirubinemia. Liver functions are otherwise normal. However, up to 2/3rd of the patients has decreased activity of Factor Vll, seen as prolonged prothrombin time.[1,2] A cardinal feature of DJS is the accumulation of dark, coarse granular pigment in the lysosomes of centrilobular hepatocytes. As a result, the liver may be grossly black in appearance. [2]

This case report documents the case of a patient with DJS who presented for emergency laparoscopic appendicectomy.

2. Case report

A 20 y, old woman weighing 60 kg was scheduled for emergency laparoscopic appendectomy. Pre–anesthetic evaluation of the patient showed increased total and direct bilirubin. Bilirubin values were raised with total bilirubin of 57.0 (normal range 3.4–20.5) µmol/L and direct bilirubin 30.5 (normal range 0.0–8.6) µmol/L, three and four folds rise respectively. CRP values too were raised at 135 mg/L, (normal values 0 – 5 mg/L) because of acute appendicitis.

CT abdomen showed normal size liver with smooth outline and homogenous parenchymal enhancement with no focal lesions.

The common bile duct and intrahepatic biliary radicles were not dilated. Portal and hepatic veins were normal.

Patient reported a similar icterus and intermittent rise in bilirubin levels during her previous pregnancy. Just before delivery her bilirubin levels were raised with total bilirubin 87 µmol/L and direct bilirubin of 55 µmol/L, four and six folds rise respectively. She was then referred to gastroenterologist and consequently

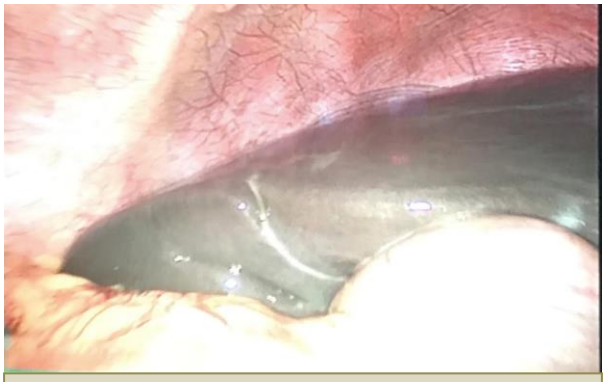

Figure 1: Laparoscopic view of the black liver of

diagnosed as DJS based on the history and investigations. However, two days after the delivery of baby, total bilirubin levels decreased to 46 μmol/L and the direct bilirubin to 22 μmol/L. Despite diagnosis she had not undergone any treatment for DJS and considered a self-limiting condition with enzymes getting back to normal.

For the laparoscopic appendicectomy, patient fasted for 8 hours and scheduled as the first case in the morning list. Intravenous infusion of 5% dextrose started at 5 am and continued during surgery. Midazolam 2 mg intravenously given in patients' holding area. Intraoperative monitoring included ECG, NIBP, pulse oximetry, capnography, and nasal temperature. Anesthetic induction included fentanyl 50 mcg, remifentanil infusion, propofol 150 mg and cis-atracurium 6 mg intravenously. Patient was intubated with size 7 cuffed endotracheal tube using GlideScope blade 3. Anesthesia maintained with 40% oxygen in air, sevoflurane, and remifentanil infusion. During laparoscopic visualization, the liver appeared dark and almost black in color (Figure 1). This is a pathognomonic sign of DJS.[2]

After removal of the appendix and deflation of the abdomen levobupivacaine 40 mg was used for local infiltration of the port wounds. Neostigmine 2.5 mg and glycopyrrolate 0.4 mg IV given to reverse residual neuromuscular blockade. The patient had a smooth extubation and painless recovery period. Patient was monitored in PACU for one hour and subsequently transferred to the standard ward.

Two days after surgery, bilirubin levels checked and a downward trend was observed with total bilirubin 44.2 μmol/L, and direct bilirubin 27.8 μmol/L.

3. Discussion.

DJS is a rare autosomal recessive disorder characterized by chronic intermittent hyper-bilirubinemia occurring in both sexes in all nationalities and races. There is 1.5 times more chances in males to be affected than females. The degree of hyperbilirubinemia may be increased by intercurrent illnesses, oral contraceptives, pregnancy and stress. [1]

Dr. Frank Johnson and Dr. Dubin discovered DJS, in 1954.[5] The main two causes of benign and inherited conjugated hyperbilirubinemia are Rotors syndrome and DJS.[6] It is associated with a defect in the ability of the hepatocytes to secrete conjugated bilirubin into the bile.[2,3] It is important to identify these syndromes to prevent misdiagnosis which may lead to unnecessary investigations.[4] A cardinal feature of DJS is the accumulation of dark coarse granular pigment in the lysosomes of centrilobular hepatocytes. As a result, the liver may be grossly black in appearance. This pigment is not melanin and is thought to be derived from epinephrine metabolites that have abnormal excretion.

In DJS, the defect in cMOAT (canalicular multi-specific organic anion transporter) protein seems to be responsible for the predominantly conjugated hyperbilirubinemia and the accumulation of pigment in the lysosomes of the hepatocytes.[1,3] The cMOAT protein is involved in energy dependent transport of certain bilirubin glucuronides and non-bile organic acids across the canalicular membrane of the hepatocytes.

Macroscopically, the liver appears grey or even black (Figure 1). Histologically, the cytoplasm of the hepatocytes contains big lysosomal granules packed with a lipochromic pigments. These were mainly located in the centrilobular region which is responsible for this color of the liver. [2, 6]

The presence of dark melanin like pigments helps differentiate DJS from Rotors syndrome.[7] The diagnostic parameters of DJS include delayed elevation of the bromo-sulfophthalein (BSP) levels post–BSP dye injection.[7] 99mTc-HIDA chole-scintigraphy shows highly disturbed excretion[8] and discharged Urine coproporphyrin with constant total volume of coproporphyrin shows more than an 80% elevation of isomer I against a decrease of isomer III.[7,9] Laparoscopic Hepatic biopsy with oral cholecystography is most useful in the diagnosis of DJS due to its effectiveness and lack of relative complications[10]. Adachi et al.[11] reported that during the last decade in Japan, 57 patients with DJS had associated cholelithiasis (14%), chronic hepatitis (10%) and hepatocellular carcinoma (3%).[7, 11]

In our patient inj. midazolam was given in the patient holding area to decrease stress. Propofol was chosen rather than thiopentone or ketamine because of its major

extrahepatic clearance.[12,13] Fentanyl 50 µg is a short acting synthetic opioid as is expected to be redistributed to muscles and the fat.

Remifentanil is an ultra-short acting drug and metabolized by blood and tissue esterases. We avoided long-acting narcotic analgesics as well as paracetamol related to their concerns in liver diseases.[14] Cis-atracurium is the preferred muscle relaxant in hepatic diseases, because of its Hoffmann degradation and ester hydrolysis.[12] Stress related bilirubin levels could explain the changes related to labour and surgery in our case. The initial increase was followed by subsequent decrease. Revising the literature, we could not find a clear evidence about the drug metabolism derangements in DJS. As the liver does not have enzyme deficiencies as in other causes of hyperbilirubinemia, the fact that the liver will affect the drug metabolism is questionable. In this case we were being cautious for concern of the patient safety and took all the measures in selecting our medications. Though in DJS, the serum bilirubin levels are raised significantly, other routine laboratory tests are normal.

4. Conclusion

Dubin Johnson Syndrome is a benign intermittent conjugated hyperbilirubinemia with normal transaminases. Hepatic interaction of anesthetic drugs needs to be further studied. However, considering the patient safety from the deleterious effect of hyperbilirubinemia especially in stress situations, safe anesthetic protocol should be employed.

5. Conflict of interests

None declared by the authors.

6. Authors' contribution

AAJ: First & corresponding author / case anesthetist
KUS: Manuscript writing / editing
MHS: Case anesthetist
IE: Administrative role/ manuscript check
LR: Reference check

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